Asbestos in the Lungs of Children

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INTRODUCTION

The extensive use of asbestos in the early part of this century has created a health hazard not only to occupationally exposed individuals, but also to the general public.[1] Asbestos is ubiquitous in our environment, and has been found in outdoor and indoor air and in drinking water supplies. In fact, asbestos bodies (AB) have been detected in the lungs of most adult urban residents upon autopsy.[2,3] Asbestos bodies are golden-brown, iron-coated asbestos fibers which are generally considered a biological marker of asbestos exposure. In animal models, structures similar to asbestos bodies have been found in association with exposure to fibrous dusts other than asbestos; hence the term "ferruginous bodies" is used when the nature of the fibrous core is not known. However, several studies have shown that, in humans, ferruginous bodies are formed on asbestos cores.[4,5] Therefore, the term asbestos bodies is used in this study for golden-brown, iron-coated fibers which show the typical segmented appearance around a central transparent core characteristic of asbestos. Other golden-brown coated fibers without the characteristic shapes or transparent cores have been considered "ferruginous bodies," formed on nonasbestos fibers.

Occupational exposure to asbestos is related to development of lung cancer, mesothelioma, asbestosis, and pleural plaques.[6,7] In some asbestos workers there is also an increased incidence of tumors of gastrointestinal tract, larynx, kidney, ovary and pancreas.[8–13] Whereas the effects of occupational exposure to asbestos are widely recognized, there is very little information available on the prevalence and effects of environmental exposure to asbestos and only recently have the effects of environmental exposure to asbestos begun to be recognized.[7,14,15]

One of the least suspected groups to be exposed to asbestos is infants and preschool children. Our studies have found asbestos bodies in the lung digests of approximately 20% of the autopsied infants and young children at our institution.[16,17] Since AB content of the lungs reflects only a small proportion of the total asbestos burden,[18] some of the infant lung digests were examined for uncoated asbestos fibers. Scanning electron microscopy examination of lung digests revealed 86 to 166 fibers per gram of wet lung. These fibers showed elemental compositions characteristic of chrysotile asbestos.[19] Further investigation of the infant lungs, using more sensitive transmission electron microscopy techniques, indicated a strikingly greater number of fibers in infant lungs than were found in the previous study. The fiber counts ranged from 214,000 to 4,900,000 fibers/g of

wet lung (unpublished data). A concomitant histologic study of the lungs revealed a mild inflammation and thickening of small airways with accumulation of macrophages in the surrounding alveoli in approximately 20% of the children.

Several questions arose from these studies: What factors predispose some infants and children to have AB and a large number of asbestos fibers in their lungs? Are those children who have AB in their lungs living in environments with higher levels of asbestos fibers or do they have underlying abnormal lung function(s) and therefore cannot clear their lungs of the inhaled fibers? Are both environmental and lung physiological factors significant in contributing to the asbestos lung burden in these children? The purpose of this study was to investigate some of these questions by examining the structural changes in children's lungs and correlating these changes with lung asbestos content.

MATERIAL AND METHODS

Lung specimens were collected from consecutive autopsies of 75 children aged 3 weeks to 25 months. All autopsies were performed at the University of Texas Medical Branch at Galveston. For each patient, 1 to 8 slides of lung, sectioned at 4 microns and processed by standard histologic techniques, were available for the study. The patient's age, sex, place of residence and diagnosis were obtained from the medical chart. If the clinical diagnosis was different from the autopsy diagnosis, the final autopsy diagnosis was used for data analysis.

Methods for AB Counts

Five grams of lung were digested in a 5.4% sodium hypochlorite solution for 24 hours. The sediment was washed in a 1 : 1 mixture of chloroform and 50% ethanol, and then centrifuged at 7,000 to 8,000 rpm. The supernatant was discarded, and the precipitate resuspended in 2 ml of 100% ethanol and filtered on a 25-mm, 0.2-micron polycarbonate filter. The filter was placed on a slide, cleared with chloroform, and prepared for light microscopic examination at ×200 to ×400 magnification. The total number of AB were determined by counting all AB on the filter and multiplying by the appropriate factor to obtain AB/5 gm of lung. All iron-coated fibers containing thin transparent cores and showing the characteristic shapes of asbestos were classified as asbestos bodies.

Methods for Uncoated Fiber Counts

Lung digests from seven infants and children were examined in a Joel 1200EX analytical electron microscope with an attached TN5500 energy dispersive X-ray analyzer at the University of Texas Health Science Center at Tyler (UTHSCT). Nuclepore polycarbonate (PC) filters (0.2 micron, 25 mm diameter) containing filtered lung digests and treated as described in the previous section received a final ethanol wash and then were carbon-coated in a Denton vacuum evaporator. The polycarbonate filter matrix was dissolved in chloroform, thus producing a clean carbon extraction replica containing the entrapped particulates and fibers.[20] Measurements and counts were conducted at 1600×, and 16,000× to 20,000× magnifications.

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TABLE 1. Demographic Data of Seventy-Five Children Studied at Autopsy for Asbestos Bodies in the Lung

Age	Males	Females	White	Black	Latin	Others	Total
Group A (3 wk.–6 mo.)	31	21	26	14	11	1	52
Group B (6 mo.–25 mo.)	10	13	11	7	5	0	23

Methods for Histological Examination

Lung sections from each patient were systematically examined and 5 to 10 bronchioles were assessed for the presence of airway inflammation. Results were recorded as 0 to ++++ inflammation, depending on the number of chronic inflammatory cells (lymphocytes and macrophages) present in the walls of the small airways. The following guidelines were used for determining the degree of inflammation in airways: 0 = no cells; + = few scattered cells; ++ = cells present in ½ to ¾ circumference; +++ = cells present in the entire circumference; ++++ = dense cellular infiltrate involving the entire circumference. The final score for bronchiolar inflammation represented the mean score of the total number of bronchioles examined in each patient. If the lungs showed bronchopneumonia, only those small airways without acute inflammation were included in the study. Sections of trachea were available for 53 of the 75 children; tracheal inflammation was assessed according to the same criteria as bronchiolar inflammation.

Statistics

Data obtained from the lung sections and from the AB counts were analyzed by Mann–Whitney U Test for ranked data using ABSTAT (Anderson Bell, Parker, CO), a statistical package for personal computers. Differences between groups of $p < 0.05$ were considered significant.

RESULTS

The demographic data on the 75 children in the study are shown in TABLE 1. The subjects were divided into two age groups of 0 (newborn) to 6 months (group A) and 7 to 25 months (group B) in order to examine the relationship between age, the number of AB, and the incidence of airway inflammation. Group A included 52 infants (31 boys and 21 girls). The youngest infant was 24 days old. Racial and ethnic distributions in this group were 26 white, 14 black, 11 Latin American, and one Asian. Group B included 23 children (10 boys and 13 girls), racial and ethnic distributions for that group were 11 white, 7 black, and 5 Latin American.

Asbestos bodies were found in the lung extracts of 11 of the group A infants (20%) and in 5 of the older group B children (22%). The distribution of AB according to age is presented in FIGURES 1 and 2. AB were found in 20% of the 1-month-old, 23% of the 2-month-old, 28.5% of the 3-month-old, 11% of the 4-month-old, and 37.5% of the 5-month-old infants. Thirty-three percent of the 7- to 9-month-old, 25% of the 9- to 12-month old, and 9% of the 12- to 24-month-old children had AB.

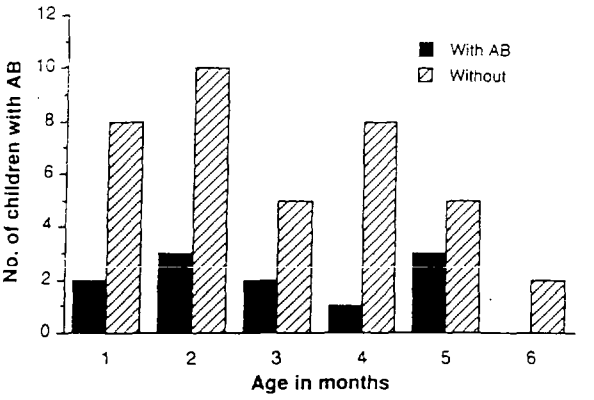

FIGURE 1. The distribution of asbestos bodies (AB) is presented in the younger children (3 weeks to 6 months old, designated group A) according to age in months. Asbestos bodies were found in the 1–5-month-old infants; no AB were found in the 6-month-old infants.

The results of uncoated fiber analysis are presented in TABLE 2. Elemental composition indicated that the fibers were mainly of the chrysotile type. Asbestos lung burdens were determined in two infants from group A and one child from group B. Two stillborn infants were included as unexposed controls, and two school age children were included to examine the effect of age on uncoated fiber content. No AB or fibers were detected in the lungs of the 28-week-gestational-age stillborn infant. The 40-week stillborn had 96,000 fibers/g wet weight. The 1.75-month-old infant and the 40-week stillborn infant had slightly longer fibers than did the older children, suggesting the possibility of fibers undergoing fragmentation with time. The 11-year-old child had three times as many fibers of same sizes as the 5-year-old did, indicating a possible cumulative effect. The largest

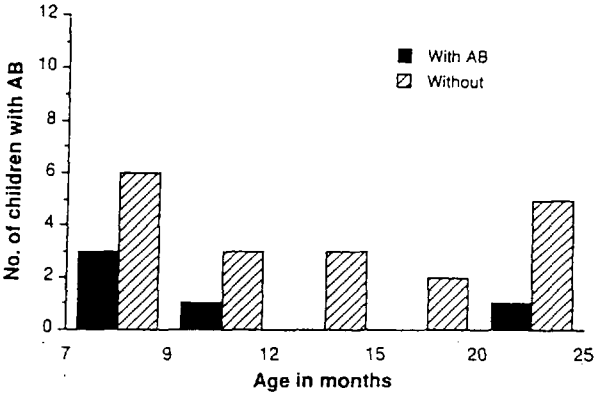

FIGURE 2. The distribution of asbestos bodies (AB) is presented in the older infants (7 to 25 months old, designated group B) according to age in months. Four of the 12 infants aged 7–12 months had AB; only one of the 11 in the 12- to 24-month-old group of children had AB.

TABLE 2. Results of Fiber Analysis in Autopsy Cases at Texas Medical Center, Galveston

Patient No.	Age	Asbestos Bodies (per 5 gm wet wt)	Fibers (per g wet wt)	Length (microns)	Width (microns)	Cause of Death
1.	0 mo	0	ND	—	—	Stillborn (28 weeks)
2.	0 mo	0	96,000	3.27	0.06	Stillborn (40 weeks)
3.	1.75 mo	0	215,000	3.00	0.05	SIDS
4.	5 mo	2	4,900,000	0.29	0.05	SIDS
5.	21 mo	0	1,200,000	1.48	0.13	MCA
6.	5 yr	0	124,000	1.23	0.12	Trauma
7.	11 yr	5	487,000	1.12	0.10	Trauma

ABBREVIATIONS: MCA, multiple congenital anomalies; SIDS, sudden infant death syndrome; ND, none detected.

number of fibers was found in the 5-month-old infant; however, these fibers were very small and suggest that fragmentation of the fibers may have occurred, resulting in a high count.

FIGURES 3 and 4 are representative examples of bronchiolar (small airway) inflammation showing +++ to + degrees of inflammation. FIGURE 5 shows an example of +++ tracheal inflammation. In addition to airway inflammation, some of the lungs showed collections of macrophages in the alveolar units surrounding

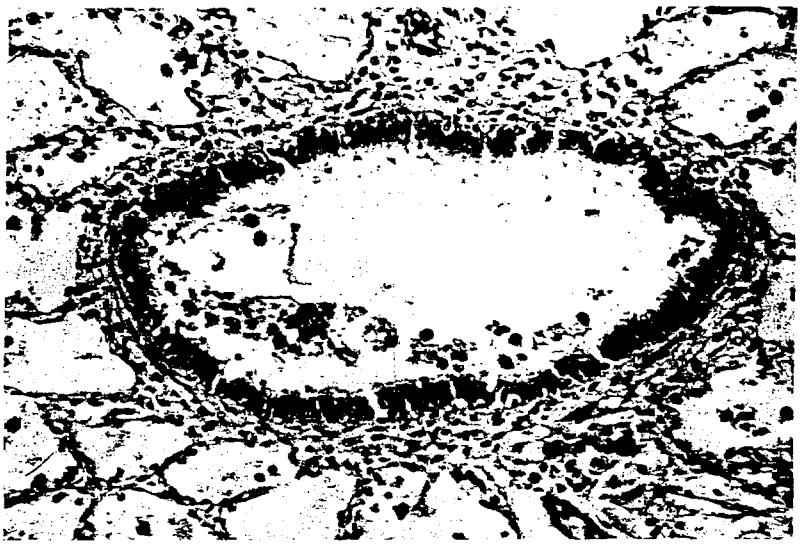

FIGURE 3. A thickened bronchiole with marked inflammation (+++) from a 1-month-old infant with AB (1 per 5 g/lung) who died of sudden infant death syndrome (hematoxylin–eosin stain; ×200).

the respiratory bronchioles, resembling the respiratory bronchiolitis seen in cigarette smokers.[21] FIGURES 6 and 7 are representative examples of the respiratory bronchiolitis observed in these children.

FIGURE 8 graphically represents the incidence of inflammation as related to age and AB content of the lungs in the 3-week to 6-month-old infants (Group A). Fifty-three percent of these infants had mild to moderate bronchiolar inflammation (+ to +++), and 83% had mild to severe tracheal inflammation (+ to ++++). FIGURE 9 graphically represents the incidence of inflammation in the 7- to 25-month-old children (group B). Mild to moderate bronchiolar inflammation (+ to +++) was present in 72% and mild to severe tracheal inflammation (+ to

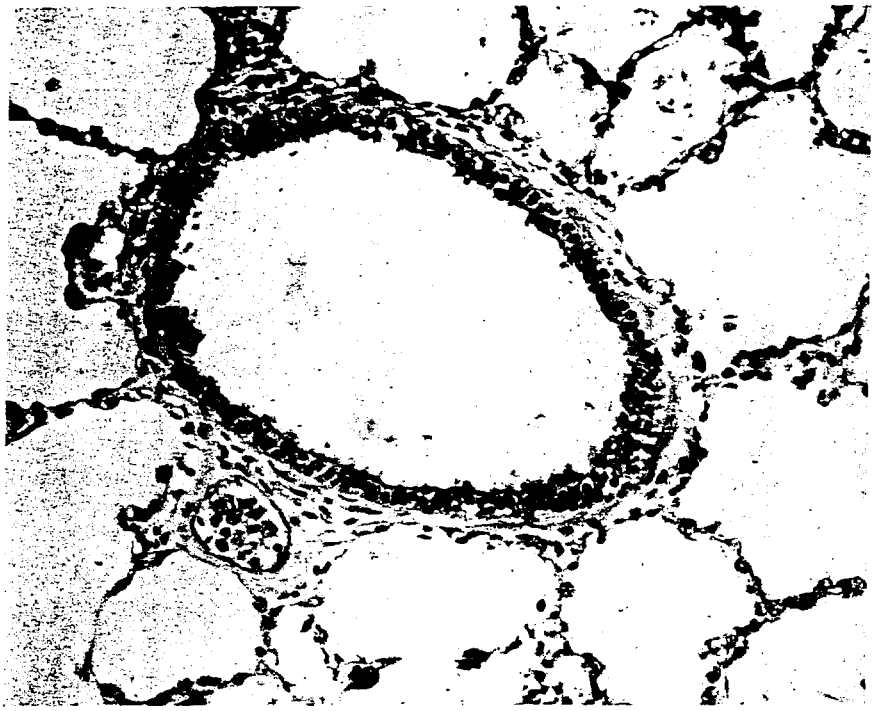

FIGURE 4. A bronchiole with mild inflammation (+) from a 10-month-old infant without AB in the lungs who died of sickle cell anemia (hematoxylin–eosin stain; ×200).

++++) was present in 99% of the older children. Respiratory bronchiolitis was present in 20% of both groups of children.

Children with AB in their lungs, irrespective of age, had a significantly greater degree ($p < 0.0085$) of tracheal inflammation than did children without AB. No significant difference was found between children with and without AB when the degree of bronchiolar inflammation was compared. When the data were examined within age groups, the children with AB in group B had a greater degree of bronchiolar inflammation than did children without AB, although the difference was statistically not significant. The children without AB in Group A exhibited

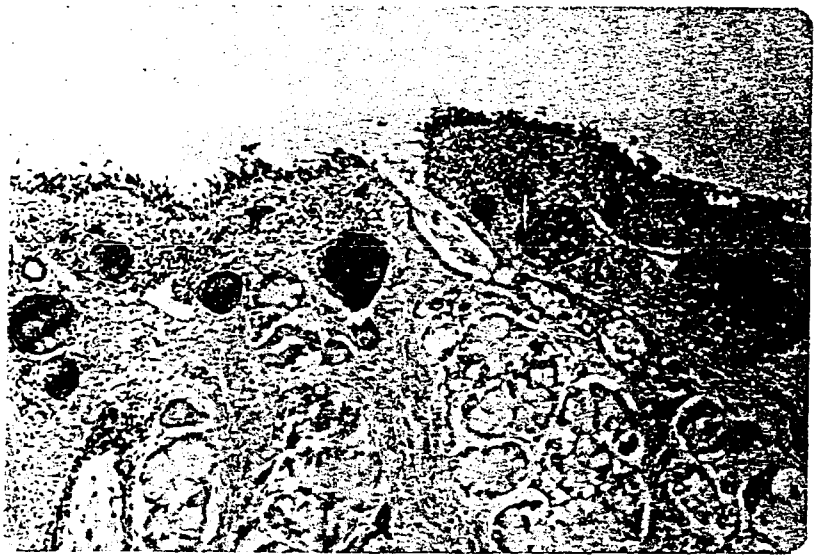

FIGURE 5. Photomicrograph of trachea shows the mucosal inflammatory infiltrate, along with congestion. The cells are a mixture of lymphocytes, macrophages, and plasma cells (hematoxylin–eosin stain; ×100).

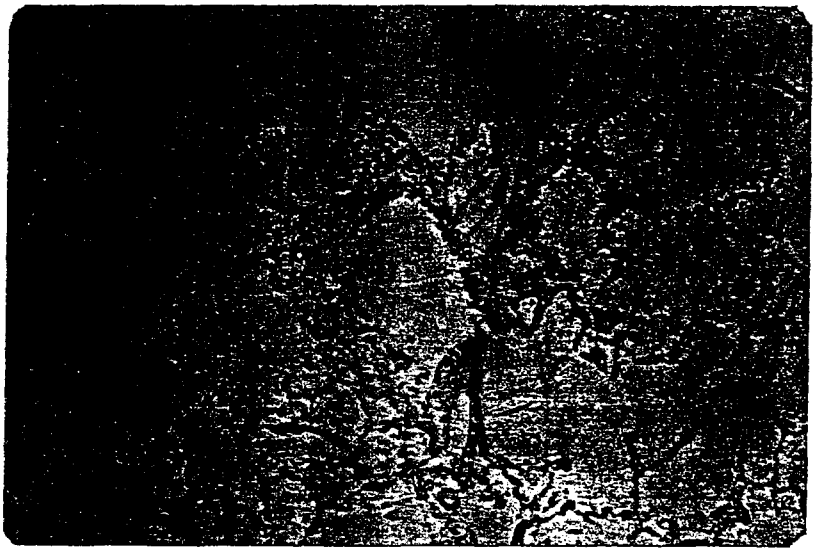

FIGURE 6. Chronic inflammatory cells in small-airway and surrounding alveoli represent respiratory bronchiolitis (hematoxylin–eosin stain; ×100).

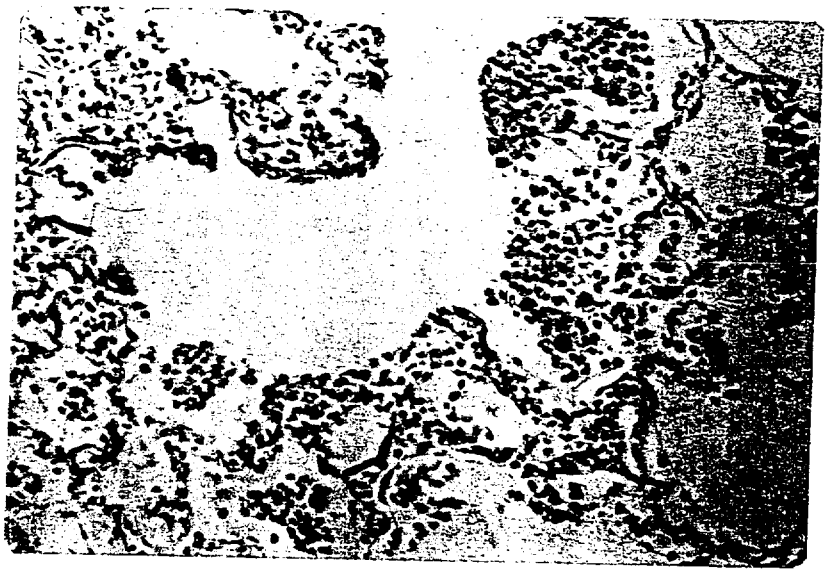

FIGURE 7. Higher magnification micrograph in a child with respiratory bronchiolitis shows the inflammatory cells, mostly macrophages (hematoxylin–eosin stain; ×200).

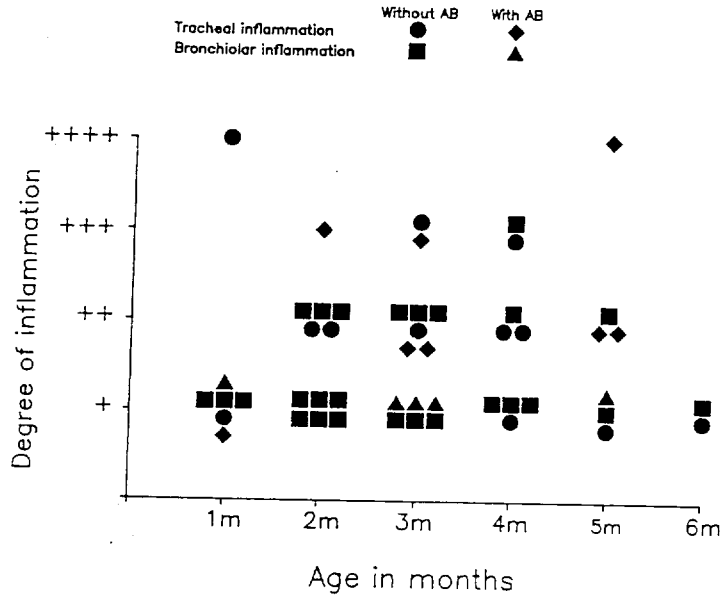

FIGURE 8. Graphic representation of the incidence and degree of bronchial and tracheal inflammation in the 3-week- to 6-month-old children with and without AB.

significantly greater degrees of bronchiolar inflammation ($p < 0.035$) than did children with AB.

DISCUSSION

Chronic asbestos exposure in humans, as well as in experimental animals, results in small-airway fibrosis with macrophage collections in the surrounding alveolar ducts.[22,23] This airway fibrosis is histologically similar to the early abnormalities seen in cigarette smokers, referred to as respiratory bronchiolitis.[21,24] The bronchiolar (small-airway) inflammation found in the lungs of children in this

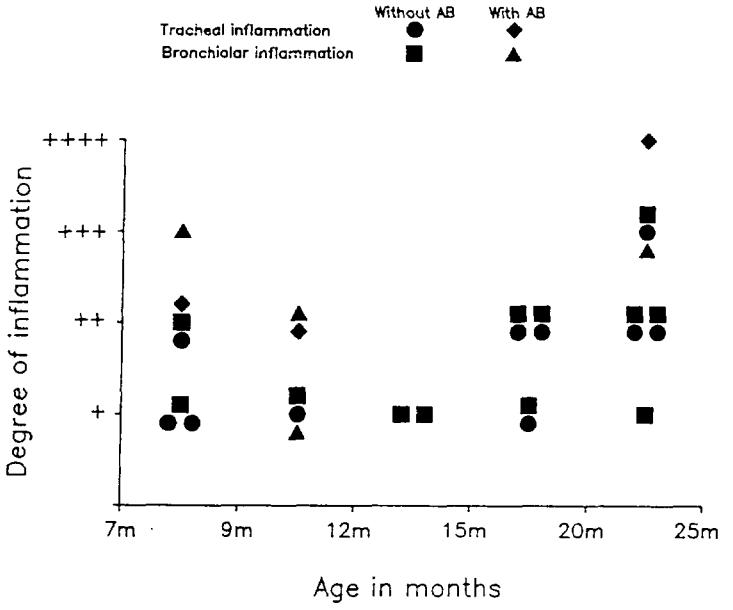

FIGURE 9. Graphic representation of the incidence and degree of bronchial and tracheal inflammation in the 7- to 25-month-old children with and without AB.

study appears similar to the respiratory bronchiolitis described in cigarette smokers and in chronic asbestos exposure. Furthermore, the degree of bronchiolar inflammation was greater in the lungs of children older than 6 months with AB compared to those without AB. These findings suggest a possible association between airway inflammation and asbestos in lungs.

The reversed significant association between bronchiolar inflammation and AB in children younger than 6 months is difficult to explain. One possibility is that asbestos bodies in young children are formed at fiber levels lower than those required to produce airway inflammation. Therefore, AB may be present in the lung digest without an associated bronchiolar inflammation. The other possibility is that these children were exposed to atmospheric pollutants and particles other than asbestos, resulting in bronchiolar inflammation without associated formation

of AB in lungs. Tracheal inflammation was present to an equal degree in both groups of children with and without AB, and may thus be related to inhalation of environmental pollutants in general. Recent studies in rats have shown increased amounts of bronchiolar inflammation after exposure to man-made as well as other types of naturally occurring fibers.[25]

An interesting finding in this study was the presence of uncoated fibers in the 40-week gestational-age stillborn infant since this infant had never breathed atmospheric air. The absence of fibers in the lungs of the 28-week stillborn infant as compared to the number of fibers present in the 40-week stillborn infant suggests that there may be transplacental transfer of asbestos fibers in the last trimester of pregnancy (28–40 weeks). The human placenta develops a greater communication between fetal and maternal circulation starting at 28 weeks of pregnancy, thus allowing circulating particles and infectious agents, for example, to enter the fetal circulation. Animal studies support this hypothesis since asbestos fibers have been demonstrated in the placenta of rats exposed to chrysotile asbestos.[26] Additionally, in an experiment on baboons, there was clear evidence of hematogenous migration of chrysotile asbestos after gavage feeding.[27]

In summary, our studies have shown that very young children are being exposed to asbestos and possibly other atmospheric pollutants. The issue of where and how the children may be exposed to asbestos needs to be addressed. Asbestos burdens in the lungs of a large cohort of children should be determined. Air and structural samples from the children's home or daycare centers should be measured for ambient levels of asbestos. Also, other possible sources of exposure should be determined through an epidemiologic survey of the parent's occupations, work environments, and smoking habits. And finally, correlational analyses should be completed to determine the degree of association between lung asbestos burdens, environmental asbestos levels, and epidemiological data in order to determine the extent and sources of asbestos exposure in children.

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